REMARKS

Rejection of Claims and Traversal Thereof

In the December 4, 2001 Office Action:

claims 62-64 were rejected under 35 U.S.C. §112, first paragraph;

claims 14-25, 27-30, 32, 34, 36, 38, 40. 42-60, 65 and 66 were rejected under 35 U.S.C. §103 (a) as being unpatentable over Donnelly, et al. (WO 96/00583) and Johnson (U.S. Patent No. 5,658,785);

claims 14-60, 65 and 66 were rejected under 35 U.S.C. §103 (a) as being unpatentable over Donnelly, et al. (WO 96/00583) and Johnson (U.S. Patent No. 5,658,785) in further view of Whittle, et al., U.S. Patent No. 5,658,785);

claims 16, 18, 20 and 50 were rejected under 35 U.S.C. §103 (a) as being unpatentable over Donnelly, et al. (WO 96/00583) and Johnson (U.S. Patent No. 5,658,785) in further view of Gissmann, et al. (WO 96/11272); and

claim 61 was rejected under 35 U.S.C. §103 (a) as being unpatentable over Donnelly, et al. (WO 96/00583) and Johnson (U.S. Patent No. 5,658,785) in further view of Stanley, et al. (U.S. Patent No. 6,096,869).

These rejections are hereby traversed and reconsideration of the patentability of the pending claims is requested in light of the following remarks.

Rejection under 35 U.S.C. §112, first paragraph

Claims 62-64 have been cancelled, thereby obviating this rejection.

Rejection under 35 U.S.C. §103 (a)

In the December 4, 2001 Office Action, claims 14-25, 27-30, 32, 34, 36, 38, 40, 42-60, 65 and 66 were rejected under 35 U.S.C. §103 (a) as being unpatentable over Donnelly, et al. in view of Johnson. Applicants submit that Donnelly, et al. in combination with Johnson does not render applicants' claimed invention *prima facie* obvious.

The present invention relates to an adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide. The fusion polypeptide comprises a structural papillomavirus polypeptide and an early non-transforming papillomavirus polypeptide having the C-terminus of the structural polypeptide connected to the N-terminus of the non-transforming polypeptide. The connection between the structural and non-transforming polypeptide is produced by ligating the 3' end of the structural ORF to the 5' end of the non-transforming ORF thereby encoding for the connected fusion polypeptide.

Donnelly, et al. teaches DNA plasmids encoding for polypeptides of papilloma virus. However, it should be noted that if more that one polypeptide is used to induce an immune response, then **separate DNA plasmids** are used as discussed on page 8, in the third paragraph of the Donnelly, et al. reference. Thus, if L1 and L2 are introduced into cells, two separate plasmids are used. The sequences encoding for the L1 and L2 structural proteins are not fused into a single plasmid. Further discussion of **separate plasmids** is located on page 9, in the second full paragraph wherein multiple constructs are discussed. Specifically, the references states that constructs encoding L1 and L2 proteins of one or more types of HPV, may be prepared, mixed and co-administered. These multiple constructs were prepared in Example 2 and co-administered in Example 4 to elicit an immune response to multiple proteins of the papilloma virus. Clearly, the combination of more than one polypeptide from different structural or early papillomavirus polypeptides inserted into a single DNA plasmid s not contemplated by Donnelly, et al.

Further, all of the DNA constructs of Donnelly, et al. use commercially available plasmids and **avoid the use of viral vectors** because as stated on page 4, first full paragraph of the Donnelly, et al. reference, retrovirus vectors have limitation that may reduce their utility as vaccines and viral vectors have inherent risks that may hinder their use in humans.

The Office contends that it would be obvious to combine the Johnston reference, which discloses the use of an adeno-associated virus (**considered a viral vector**), with the teachings of Donnelly, et al. and that the combination renders applicants' claimed invention obvious. Applicants vigorously disagree.

In order to determine obviousness, it is incumbent upon the Office to view the applicants' invention as a whole. *In re Wesslau*, 174 U.S.P.Q. 393 (C.C.P.A. 1965). Concurrently, the Office must consider the teaching of any cited references in their respective entireties. Certain individual features from the references may not be arbitrarily chosen (while arbitrarily discarding other closed features) to merely lump together disparate features of different references as a mosaic in an attempt to meet the features of the rejected claims. For instance, why would anyone reading Donnelly, et al. look to Johnson for a viral vector when in fact Donnelly, et al. avoids the use of viral vectors as expressly stated on page 4, line 5 to 14 of the Donnelly reference. Clearly, this statement made by Donnelly, et al. cannot be ignored by the Office. As a matter of fact, this specific statement in the Donnelly, et al. reference teaches away from using a viral vector such as that disclosed in the Johnson reference.

Obviousness cannot be established by combining the teachings of the cited references to produce the claimed invention, absent some teaching or suggestion supporting the combination and suggesting the desirability of the combination. According to the board in Ex parte Humphreys, 24 U.S.P.Q.2d 1255, 1262 (B.P.A.I. 1992) the Office was wrong in rejecting the claims for obviousness because the examiner's rejection was not specific as to how one of ordinary skill in the art would have found it obvious to combine the references. Furthermore, they noted the examiner had not explained with any **specificity what areas of the references would suggest the combination.**

This is the circumstances here. The Office has not identified any objective or specific teachings or suggestions in the cited references that would motivate one skilled in the art to combine the references. Thus, the Office seems to be merely reinterpreting the prior art in light of applicants' disclosure, in order to reconstruct applicants' claimed invention, but without any instructional or motivating basis in the references themselves. Such approach is improper and legally insufficient to establish any *prima facie* case of obviousness.

The Office proposes that the two references can be combined to teach and suggest applicants' claimed invention. However, even if the two references were attempted to be combined (despite the absence of any proper basis for such combination), the resultant combination would still not embody every limitation required by applicants' claimed invention. Specifically, the combination would still **not** include a fusion polypeptide comprising a structural papillomavirus polypeptide and an early non-transforming papillomavirus polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide. The connection between the structural and non-transforming polypeptide is produced by ligating the 3' end of structural ORF to the 5' end of the non-transforming ORF, all of which is recited in the claimed invention.

In light of the above discussion and the fact that (1) there is no motivation, suggestion or teaching to combine the references; (2) each and every recited limitation of applicants' claimed invention are not disclosed or suggested in the cited references; and (3) even if the references were combinable the primary reference Donnelly, et al. teaches away from the use of a viral vector such as that disclosed in the Johnson reference; it is clear that the cited combination fails to establish a *prima facie* case of obviousness of applicants' claims as herein amended.

The Office further rejected claims 14-60, 65 and 66 under 35 U.S.C. §103 (a) over Donnelly, et al. and Johnson, as above, in further view of Whittle, et al. Regardless, of the teachings of Whittle, et al., applicants respectfully submit that the defects in the alleged *prima facie* case over Donnelly, et al. and Johnson are not cured by the addition of Whittle, et al.

Whittle, et al. teaches fused polypeptides of HPV but the expression of the fused polypeptides is clearly set forth as a technique which can enhance and achieve high level of expression in heterologous cells, in particular *E. coli* bacterial cells. Whittle, et al. preferably uses the T7 expression system of *E coli* wherein recombinant polypeptides are found in insoluble aggregates within the cell. Moreover, the Whittle, et al. reference specifically discloses a method of preparing a suitable vector for expression of the polypeptide in *E. coli* bacteria cells by inserting a nucleic acid sequence which encodes the desired polypeptide but which has been mutated such that codons or groups of codons which cause premature termination of transcription or translation have been replace by degenerate codons. The reference discloses that by using the T7 expression system, the incidence of premature termination of transcription can effectively be prevented or reduced by

removal of at least one poly-T sequence such as [TTT]n, by replacing such a sequence with an acceptable alternative, e.g. a [TTC]n sequence which encodes the same amino acids, leading to a higher yield of desired polypeptide. All the examples in the Whittle, et al. reference demonstrate the use of the T7 expression system.

As stated above, it is incumbent on the Office to provide some suggestion or teaching in the cited reference that would lead one skilled in the art to proceed in the direction of applicants' claimed invention. What is the asserted motivation in Whittle, et al. or Donnelly, et al. to use an adeno-associated virus vector with a HPV fused polypeptide? Especially because Donnelly, et al teaches away from the use of a viral vector and Whittle, et al. provides guidance for only the T7 expression system. The Courts have addressed this issue numerous times and have stated that "[t]he mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification." *In re Mills*, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). Thus, this allegedly "obvious" direction is supported only by the Office's reinterpretation of the art in light of applicants' disclosure.

Claims 16, 18, 20 and 50 were rejected under 35 U.S.C. §103 (a) as being unpatentable over Donnelly, et al. and Johnson in further view of Gissmann, et al. Regardless, of the teachings of Gissmann, et al., applicants respectfully submit that the defects in the alleged *prima facie* case over Donnelly, et al. and Johnson are not cured by the addition of Gissmann, et al.

The Office must view Gissmann, et al. in its entirety and if properly viewed, the cited reference in combination with the primary and secondary references still do not teach or suggest all the claimed limitations of the present invention. Gissmann, et al. discloses fused polypeptides wherein a portion of a viral structural proteins of HPV, whether L1 or L2, is deleted. In the deleted area of the sequence another sequence is inserted. This is in sharp contrast to Donnelly, et al. that expressly states that maintaining the conserved portions of the papilloma viruses, such as structural portions L1 and L2, is important to provide protection against subsequent challenges by different types of papilloma viruses. Donnelly, et al. maintains the integrity of the structural proteins for the specific reason of providing extended protection even if a subsequent attack occurs by another virus strain. Clearly mutating the L1 or L2 structural gene is discouraged by Donnelly, et al. and as such the Gissmann, et al and Donnelly, et al. references are not combinable. More important, if the mutation of L1 and L2 as taught by Gissmann, et al. is introduced into the DNA constructs of

Donnelly, et al. the intended purpose of maintaining a highly conserved structural protein in the Donnelly, et al. reference is destroyed. Thus, there is no motivation to combine the cited references and the Office has not provided any teachings or suggestions sufficient to provide one skill in the art the motivation to make the proposed modifications needed to arrive at applicants' claimed invention.

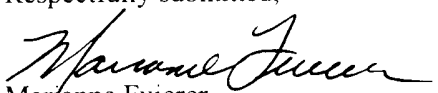
Claim 61 was rejected under 35 U.S.C. §103 (a) as being unpatentable over Donnelly, et al. and Johnson in further view of Stanley, et al. Regardless of the teachings of Stanley, et al. applicants respectfully submit that the defects in the alleged prima facie case over Donnelly, et al. and Johnson are not cured by the addition of Stanley, et al. Thus, for reasons set forth above, this rejection also is improper.

In light of the foregoing observations and the clarifying amendments to the claims, applicants submit that the cited references fail to suggest the subject matter of the rejected claims. Reconsideration and withdrawal of the rejections is respectfully requested.

Conclusion

Applicants have satisfied the requirements for patentability. All pending claims are free of the art and fully comply with the requirements of 35 U.S.C. §112. It therefore is requested that Examiner Woitach reconsider the patentability of claims 14-61, 65-66, in light of the distinguishing remarks herein and withdraw all rejections, thereby placing the application in condition for allowance. Notice of the same is earnestly solicited. In the event that any issues remain, Examiner Andres is requested to contact the undersigned attorney at (919) 419-9350 to resolve same.

Respectfully submitted,



Marianne Fuierer
Registration No. 39,983
Attorney for Applicant

INTELLECTUAL PROPERTY/
TECHNOLOGY LAW
P.O. Box 14329
Research Triangle Park, NC 27709
Telephone: (919) 419-9350
Fax: (919) 419-9354
Attorney Ref: 4121-107

APPENDIX A

In the Claims

Please amend claims 14, 49, 50, 51, 52, 53, 61 and 65 to read as follows:

14. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of L1-ORF, L2-ORF and fragments of any of the foregoing ORFs; and

an early papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early papillomavirus polypeptides or fragments thereof are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of the non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

49. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of L1-ORF and L2-ORF; and

an early human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF and E7-ORF, wherein said early human papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of the non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

50. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of L1-ORF and L2-ORF; and

an early human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF and E7-ORF, wherein said early human papillomavirus peptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of the non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide, and the human papillomavirus of (a) and (b) is selected from the group consisting of HPV 16, HPV 18, HPV 33, HPV 35 and HPV 45.

51. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by L1-ORF or a fragment thereof; and

an early human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early human papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of the non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

52. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by an HPV16 or 18 L1-ORF or a fragment thereof; and

an early human papillomavirus polypeptide encoded by an HPV 16 or 18 open reading frame selected from the group consisting of E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early human papillomavirus polypeptides are non-transforming, and wherein

the 3' end of the structural ORF is ligated to the 5' end of the non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

53. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by HPV16 or 18 L1-ORF; and

an early human papillomavirus polypeptide encoded by an HPV 16 or 18 open reading frame selected from the group consisting of: E6-ORF and E7-ORF, wherein said early papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of the non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

65. (Twice Amended) A method for activating an immune system of a subject comprising administering to the subject an adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: L1-ORF, L2-ORF and fragments of any of the foregoing ORFs; and

an early papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of the non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

APPENDIX B

14. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of L1-ORF, L2-ORF and fragments of any of the foregoing ORFs; and

an early papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early papillomavirus polypeptides or fragments thereof are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of the non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

15. The vector of claim 14 wherein the structural papillomavirus polypeptide is an HPV polypeptide.

16. The vector of claim 15 wherein the HPV is selected from the group consisting of HPV 16, HPV 18, HPV 33, HPV 35 and HPV 45.

17. The vector of claim 14 wherein the early papillomavirus polypeptide is an HPV polypeptide.

18. The vector of claim 17 wherein the HPV is selected from the group consisting of HPV 16, HPV 18, HPV 33, HPV 35 and HPV 45.

19. The vector of claim 14 wherein both the structural papillomavirus polypeptide and the early papillomavirus polypeptide are HPV polypeptides.

20. The vector of claim 19 wherein the HPV is selected from the group consisting of HPV 16, HPV 18, HPV 33, HPV 35 and HPV 45.

21. The vector of claim 14 wherein the nucleotide sequence is under the control of a constitutive promoter.

22. The vector of claim 14 wherein the nucleotide sequence is under the control of an inducible promoter.

23. The vector of claim 14 wherein the nucleotide sequence is under the control of a tissue-specific promoter.

24. The vector of claim 14 wherein the nucleotide sequence is under the control of a tumor-specific promoter.

25. The vector of claim 14 wherein the structural papillomavirus polypeptide is encoded by L1-ORF.

26. The vector of claim 14 wherein the structural papillomavirus polypeptide is encoded by a fragment of L1-ORF.

27. The vector of claim 14 wherein the structural papillomavirus polypeptide is encoded by L2-ORF.

28. The vector of claim 14 wherein the structural papillomavirus polypeptide is encoded by a fragment of L2-ORF.

29. The vector of claim 14 wherein the structural papillomavirus polypeptide is encoded by HPV 16 L1 ORF.

30. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by E1-ORF.

31. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by a fragment of E1-ORF.

32. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by E2-ORF.

33. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by a fragment of E2-ORF.

34. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by E4-ORF.

35. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by a fragment of E4-ORF.

36. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by E5-ORF.

37. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by a fragment of E5-ORF.

38. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by E6-ORF.

39. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by a fragment of E6-ORF.

40. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by E7-ORF.

41. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by a fragment of E7-ORF.

42. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by HPV 16 E6-ORF.

43. The vector of claim 14 wherein:
the early papillomavirus polypeptide is encoded by E6-ORF or a fragment thereof; and
structural papillomavirus polypeptide is encoded by L2-ORF or a fragment thereof.

44. The vector of claim 14 wherein:
the early papillomavirus polypeptide is encoded by HPV 16 E7-ORF or a fragment thereof; and
structural papillomavirus polypeptide is encoded by HPV 16 L2-ORF or a fragment thereof.

45. The vector of claim 14 wherein:
the early papillomavirus polypeptide is encoded by HPV 16 E6-ORF or a fragment thereof; and
structural papillomavirus polypeptide is encoded by HPV 16 L2-ORF or a fragment thereof.

46. The vector of claim 14 wherein:
the early papillomavirus polypeptide is encoded by HPV 16 E7-ORF or a fragment thereof; and
structural papillomavirus polypeptide is encoded by HPV 16 L2-ORF or a fragment thereof.

47. The vector of claim 14 wherein:
the early papillomavirus polypeptide is encoded by HPV 18 E6-ORF or a fragment thereof; and
structural papillomavirus polypeptide is encoded by HPV 18 L2-ORF or a fragment thereof.

48. The vector of claim 14 wherein:
the early papillomavirus polypeptide is encoded by HPV 18 E7-ORF or a fragment thereof; and
structural papillomavirus polypeptide is encoded by HPV 18 L2-ORF or a fragment thereof.

49. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of L1-ORF and L2-ORF; and

an early human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF and E7-ORF, wherein said early human papillomavirus polypeptides are non-transforming, and wherein the 3' end of the

structural ORF is ligated to the 5' end of the non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

50. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of L1-ORF and L2-ORF; and

an early human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF and E7-ORF, wherein said early human papillomavirus peptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of the non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide, and the human papillomavirus of (a) and (b) is selected from the group consisting of HPV 16, HPV 18, HPV 33, HPV 35 and HPV 45.

51. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by L1-ORF or a fragment thereof; and

an early human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early human papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of the non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

52. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by an HPV16 or 18 L1-ORF or a fragment thereof; and

an early human papillomavirus polypeptide encoded by an HPV 16 or 18 open reading frame selected from the group consisting of E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early human papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of the non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

53. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by HPV16 or 18 L1-ORF; and

an early human papillomavirus polypeptide encoded by an HPV 16 or 18 open reading frame selected from the group consisting of: E6-ORF and E7-ORF, wherein said early papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of the non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

54. The vector of claim 53 wherein the ORFs of (a) and (b) are HPV 16 ORFs.

55. The vector of claim 53 wherein the ORFs of (a) and (b) are HPV 18 ORFs.

56. The vector of claim 53 wherein:
the ORFs of 53(a) and 53(b) are HPV 16 ORFs; and
the early human papillomavirus polypeptide is encoded by E6-ORF.

57. The vector of claim 53 wherein:
the ORFs of 53(a) and 53(b) are HPV 18 ORFs; and
the early human papillomavirus polypeptide is encoded by E6-ORF.

58. The vector of claim 53 wherein:
the ORFs of 53(a) and 53(b) are HPV 16 ORFs; and
the early human papillomavirus polypeptide is encoded by E7-ORF.

59. The vector of claim 53 wherein:
the ORFs of 53(a) and 53(b) are HPV 18 ORFs; and
the early human papillomavirus polypeptide is encoded by E7-ORF.

60. A vaccine composition comprising:
the vector of claim 14; and
an auxiliary agent.

61. The vaccine composition of claim 49 further comprising one or more immune system-activating agents.

65. (Twice Amended) A method for activating an immune system of a subject comprising administering to the subject an adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: L1-ORF, L2-ORF and fragments of any of the foregoing ORFs; and

an early papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of the non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

66. The method of claim 65 wherein the fusion polypeptide is administered as a component of a vaccine composition.